DIETHYL ETHER EXPOSURE OF EEG TECHNICIANS USING COLLODIAN

by

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SUPERVISORY COMMITTEE APPROVAL

of a thesis submitted by

Jeri L. Lockman

This thesis has been read by each member of the following supervisory committee and by majority vote has been found to be satisfactory.

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I have read the thesis of Jeri L. Lockman in its final form and have found that (1) its format, citations, and bibliographic style are consistent and acceptable; (2) its illustrative materials including figures, tables, and charts are in place; and (3) the final manuscript is satisfactory to the Supervisory Committee and is ready for submission to the Graduate School.

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ABSTRACT

The purpose of this study was to determine if EEG technicians using collodian are exposed to diethyl ether and to determine if there was an accumulation of ether in the body after repeated exposures. Breathing zone air and expired-air samples were collected on four EEG technicians for five consecutive days. Expired-air samples were also collected the following Monday morning.

Measurable amounts of ether were found in all samples collected from the subjects. No relationship was found between the levels of ether in the breathing zone and levels found in the individual subject's expired-air. Also, levels of ether in the expired-air did not increase over the week nor was there any consistent increase in levels at the end of the day immediately after exposure as compared to the morning level. The scatter diagram of the number of EEGs performed and the levels of ether in the breathing zone indicate a positive trend between these two factors.

It can be concluded from this study that EEG technicians are exposed to diethyl ether via collodian use. It can also be concluded that a body burden exists in

EEG technicians with repeated exposure to low concentrations of ether. Expired-air sample results were considered invalid because of analytical problems. For this reason, no conclusions can be drawn regarding a relationship between exposure levels and expired-air levels of ether, nor can any statement be made regarding the accumulation of ether in the body with repeated exposures.

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CHAPTER I

INTRODUCTION

Collodian is a substance containing 4% dinitrocellulose, 24% ethyl alcohol, and 70% diethyl ether (Gosselin, Hodge, Smith & Gleason, 1976). It is a thick, colorless liquid with an ether-like odor (U.S. Coast Guard [Chris], 1978). It is used to adhere electroencephalogram electrodes to the scalp. The solvent mixture of diethyl ether and ethyl alcohol is reportedly the chief source of toxicity in collodian (Gosselin et al., 1976). Collodian making is recognized as an occupation in which exposure to diethyl ether may occur (Occupational Diseases, A Guide to Their Recognition, Department of Health, Education and Welfare, 1977). However, EEG technicians using collodian are not included in the list of occupations with a potential exposure risk to diethyl ether.

Problem

Diethyl ether is a chemical that has been reported to have biological effects on animals and humans which have been exposed to it. EEG technicians represent an occupation associated with a potential exposure to

chronic low levels of diethyl ether.

Purpose

The purpose of this study was to determine if EEG technicians are indeed exposed to low doses of diethyl ether. The study was not intended to look at the long term effects of such an exposure but rather to ascertain if the exposure exists. In addition, this study will determine whether a body burden exists from chronic exposure to ether as demonstrated by detectible levels of ether in the expired air; and if so, whether there is a correlation between exposure levels and expired air levels of ether.

CHAPTER II

LITERATURE REVIEW

The occupational standard of diethyl ether as promulgated by the Occupational Safety and Health Administration is 400 ppm (1200 mg/m^3) for an 8-hour time-weighted average concentration basis. This standard was adopted from the recommendations of the American Conference of Governmental Industrial Hygienists (ACGIH) and was based on the prevention of nasal irritation and possible narcosis (NIOSH criteria, 1977). The most current ACGIH threshold limit value (TLV) for ethyl ether remains at 400 ppm or 1200 mg/m^3, with an associated 500 ppm or 1500 mg/m^3 Short-Term Exposure Limit. In 1974, the Hospital Engineering Cooperative Groups of Denmark recommended that the highest permissible average concentration of diethyl ether in the breathing zone be 3 ppm or 9 mg/m^3 (NIOSH document, 1977). They state that since the lowest concentration of anesthetic gases which offers any risk upon long-term exposure is unknown it is necessary to attempt to remove all excesses (NIOSH document, 1977). NIOSH recommended that occupational exposure to waste gases, including diethyl ether, from anesthetic procedures be controlled

in order to minimize potential adverse effects on the health and safety of workers and their unborn children. Studies to determine these adverse effects will be discussed in depth later in this review.

Biotransformation

Diethyl ether [$(C_2H_5)_2$=0] is a colorless, highly volatile liquid with a boiling point of 35° C. It possesses a pungent odor and gives off an irritating vapor (Goodman & Gilman, 1970). Diethyl ether has enjoyed long clinical and industrial use; however, there are a number of significant gaps in our knowledge of this substance and little information about its elimination or metabolism is available.

Until the late 1960s, ethyl ether was considered to be eliminated unchanged from the body. Haggard (1924) studied the recovery of diethyl ether from the expired air of dogs. He found that an average of 87% of the administered amount was recovered unchanged in the expired air. Onchi and Asao (1961) studied the recovery rate of diethyl ether in human subjects using lower percentages of ether. Ether was administered by inhalation, and then expired air was collected for three consecutive 40-minute periods. In the first subject, the amount eliminated in 120 minutes was 83.9% of the amount absorbed in the 20 minutes of inhalation. In the second and third subjects, the amounts recovered

in 120 minutes were lower, being 49.9% and 37%, respectively. The two explanations offered by Onchi and Asao for the difference in recovery rate as compared to Haggard's findings included a difference in the sizes of dogs and human subjects and the difference in the concentration of the ether vapor used.

The metabolic pathways for the degradation of diethyl ether have not been worked out in detail. The cleavage of ether by the biological system was established by Axelrod (1956) but beyond this we know little about the biotransformation of diethyl ether. Van Poznak (1974) postulated that an aldehyde intermediate is formed following ether cleavage. The aldehyde so formed may then undergo reduction to ethanol or oxidation to carbon dioxide or both in the Krebs cycle (see Figure 1).

In 1978, Aune, Ranek, Bessesen and Midrland, measured blood-acetaldehyde concentrations in patients to determine if concentrations were affected by ether anesthesia. Findings of the study showed that a compound behaving like acetaldehyde in the chromatographic system appeared during ether anesthesia and no blood-acetaldehyde increase was seen in patients not receiving ether. This study would appear to validate the postulation that an aldehyde intermediate is formed following ether cleavage.

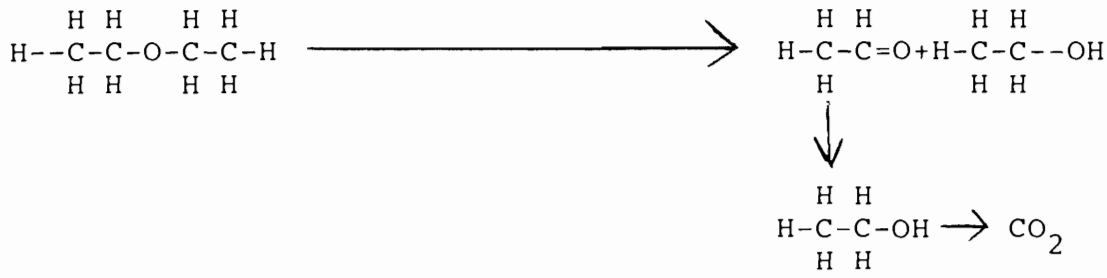

Figure 1. Biotransformation of diethyl ether.

Van Dyke, Chenoweth and Van Poznak (1964) studied the fate of diethyl-1-^{14} C-ether in rats. The ether was administered by intraperitoneal injection. Four percent of the total radioactivity injected was collected over a 24-hour period as $^{14}CO_2$, and during the same period an additional 2% was recovered as nonvolatile radioactivity in the urine. A portion of the administered ether was also stored in the fat and released slowly. As this slow release occurred, the amount of ether in the animal was maintained at a constant, although low level.

Cohen and Hood (1969) following autoradiographic studies in mice observed that initially ether was uniformly distributed throughout the tissue slice. After 2 hours, most of the radioactivity had disappeared but some was still present in liver, kidney, intestine and the nasal mucous membranes. When these tissue slices were heated to drive off volatile ^{14}C compound, radioactivity was still seen to be present in the liver and intestines. The extracts from the liver were then separated by thin-layer chromatography. Exposure to photographic film established the presence of a nonvolatile radioactive metabolite. Following exposure of these metabolites to B-glucuronidase, they performed repeat radiochromatography and the major metabolic factor was identified as a glucoronide of ether. The appearance

of $^{14}CO_2$ could be explained by the breakdown of diethyl ether through the addition of a hydrosyl group to form ethyl alcohol and acetaldehyde. Additional pathways are required to account for the presence of other non-volatile metabolites (Geddes, 1972). No information was available regarding the biological half-life of diethyl ether.

In the study conducted by Onchi and Asao (1961), two phases of ether elimination were described. The first was a rapid phase followed by a phase of slow decrease. They found that traces of ether were detectable by gas-chromatography in the expired air until 20 hours after inhalation of ether. A diagram of ether elimination from that study is shown in Figure 2. Figure 3 demonstrates yolk concentration during uptake and excretion of 13% ether in 3-day living embryos (Smith, Caub & Lehrer, 1972).

Effects of Diethyl Ether

Much of the data on the effects of diethyl ether exposure either have been obtained by studying patients who experienced some type of complication following clinical anesthesia or by evaluating the effects of diethyl ether as an anesthetic. These studies do give us information about the acute, high dose effects of ether on humans. Stevens, Eger, Joas, Cromwell, White and Dolan (1973) studied the effects of various anes-

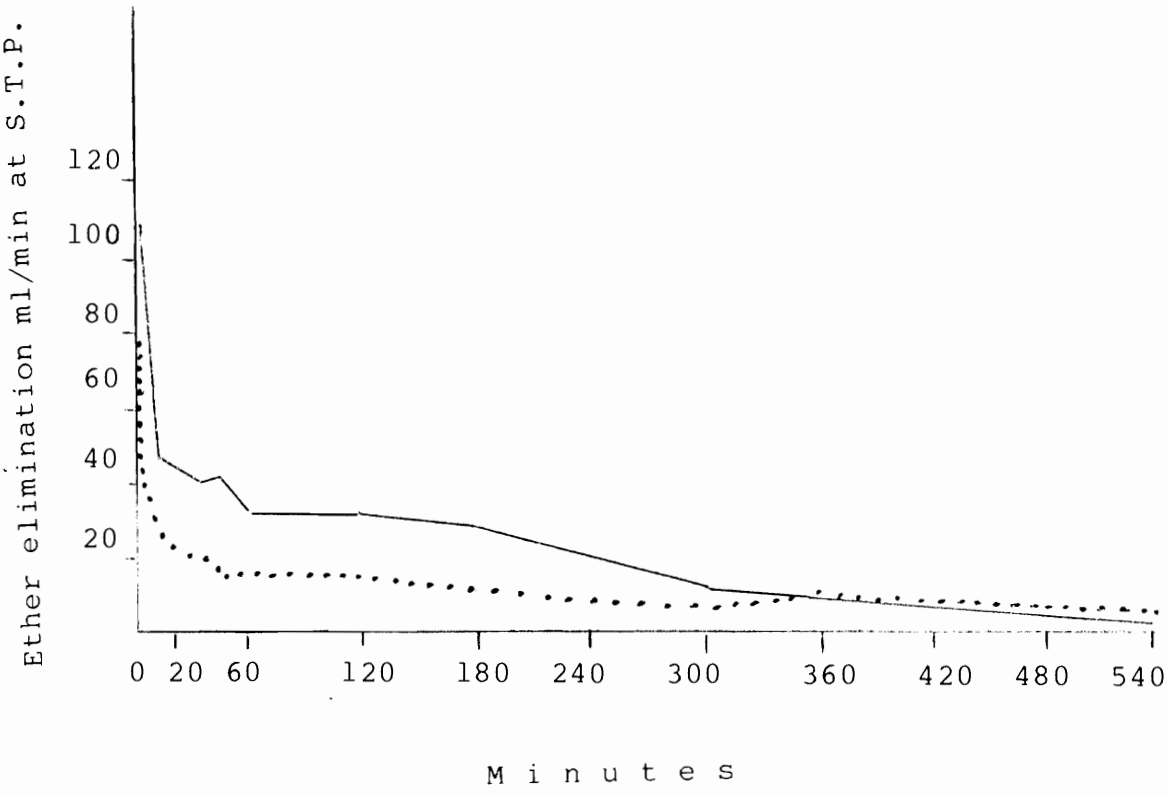

Figure 2. Ether elimination results. Adapted from Onchi & Asao, 1961).

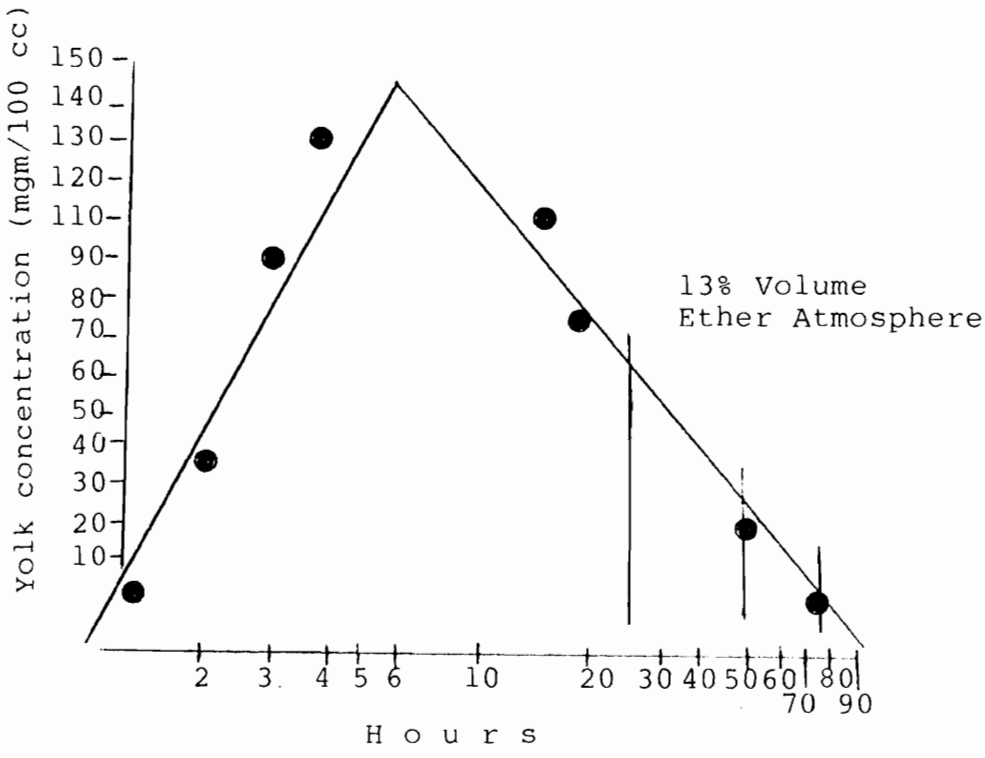

Figure 3. Uptake and elimination of ether in chick embryos. Adapted from Smith et al., 1972.

thetics including a diethyl ether on cardiorespiratory, renal and hepatic function using young, healthy human volunteers. In the ether group, blood urea nitrogen (BUN) decreased significantly but returned to control values within 7 days; potassium values increased on the seventh day; and bicarbonate content tended to increase on the first day after anesthesia and continued to increase further at 7 days.

Oyama and Takazawa (1971) explored the effects of ether during anesthesia on carbohydrate and fat metabolism by measuring plasma growth hormone (HGH), insulin, blood glucose, free fatty acid (FFA), and cortisone, using 20 male patients between the ages of 22-56 years. The plasma HGH concentration during ether anesthesia showed a significant elevation 1 hour after the start of the operation. There was a relative decrease in plasma insulin level; increases in blood glucose and the plasma cortisol level significantly increased. There was no demonstrable variation of blood FFA.

Rosenmann, Dishon, Durst and Boss (1972) reported that ether anesthesia causes vasoconstriction in the wake of which minor morphological changes ensue. Though ether, per se, is not considered to be hepatoxic, its administration is accompanied by mild hepatic functional derangements with or without minimal cytological evidence of injury. While agreeing that ether is not a

true hepatoxin, other investigators have described alterations in liver histology (i.e., reduced glycogen content, slight fatty changes, and central necrosis) (Adrian, 1970; Robertson, 1959).

Epidemiologic Studies

Several epidemiologic studies have been conducted in an attempt to identify the health effects associated with chronic exposure to waste anesthetic gases. However, none of the studies provided information on the anesthetic agent or on the concentrations of the gases present.

NIOSH (NIOSH criteria, 1971, p. 29) reports:

> In 1966, Vaisman surveyed by questionnaire 303 Russian anesthesiologists (193 men and 110 women). Ninety-eight percent reported using diethyl ether; 59% nitrous oxide; 28% halothane; and 21% other agents. A high incidence of headache, fatigue, irritability, nausea, and itching was reported. The authors also noted that 18 of 31 pregnancies among anesthesiologists who were between the ages of 24 and 38 ended in spontaneous abortions. In addition, there were two premature births and one child was born with a congenital malformation. The anesthesiologists with abnormal pregnancies had exposure of 25 hours per week or more while those with normal pregnancies did not exceed 15 hours per week.

Other epidemiologic studies will not be reviewed here because they give us no information regarding the agents used. However, the study discussed above suggests that chronic exposure to low concentrations of anesthetic

gases, which include diethyl ether, may have deleterious effects on the health of workers.

Animal Studies

In order to determine teratogenic effects of diethyl ether, Smith et al. (1972) conducted studies on chicken embryos exposed to varying levels of ether during incubation. The mortality and anomaly rates of chick embryos after exposure to ether atmospheres are shown in Table 1. The types of anomalies produced by exposure to ether on the third and fourth day generally were similar both in type and incidence (see Table 2). However, the incidence of eye anomalies was 30.4% after all ether treatments. Only 8% of the anomalies encountered in 1,110 control eggs during this same period were of the eye. Defects included anophthalmia, and microphthalmia. This study demonstrated the teratogenic capability of diethyl ether in the vertebrate, although the exact mechanism for that effect is not known (Smith et al., 1972).

Stevens et al. (1975) reported the effects of 35-day exposures to subanesthetic concentrations of diethyl ether in mice, rats and guinea pigs which were in a phase of rapid body growth. Diethyl ether reportedly had a negligible effect on rat or mouse weight gain and a detrimental effect in guinea pigs at the one percent dose. Although no hepatic injury was seen with

Table 1

Toxicity of Diethyl Ether in the Chick Embryo

Incubation Day	Tests N	Duration	Concentration of Ether	Total Embryos	Dead embryos No. dead	Dead embryos % dead	Survivors Total	Survivors % surviving	Anomalous Survivors Total	Anomalous Survivors %
		hr	%							
1	1	6	20	23	1	4.5	22	95.5	3	13.7
	Air controls			20	0	0	20	100	0	0
2	2	5	20	34	3	7.0	31	93.0	4	12.9
	Air controls			15	1	6.7	14	93.3	0	0
3	5	6	10	153	14	9.2	139	90.8	0	0
	5	6	13	138	32	23.1	106	76.9	15	14.1
	3	6	17	108	73	67.6	35	32.4	3	8.5
	3	5	20	93	74	79.6	19	20.4	10	52.6
	3	6	20	102	98	96.1	4	3.9	1	25
	1	6	30	53	53	100	0	0	0	0
	Air controls			372	7	1.9	365	97.8	4	1.1
4	3	5	11	72	29	40.3	43	59.7	9	20.9
	3	6	9	94	47	50.0	47	50.0	5	10.6
	6	6	13	188	126	67.6	62	32.4	5	8.1
	Air controls			134	1	0.7	133	99.3	1	0.8

Note. Adapted from Smith et al., 1972.

Table 2

Types of Anomalies in the Chick After Exposure to Ether

Type	3 days N	3 days % anomaly	4 days N	4 days % anomaly	Total N	Total %	Control[a] N	Control[a] % anomaly
Brain	12	22.7	2	12.5	14	20.3	3	23.0
Eyes	13	22.8	8	50	21	30.4	1	8.0
Beak	12	22.7	4	25.0	16	23.2	3	23.0
Extremities	6	11.3	0	0	6	8.7	1	8.0
Body	10	18.8	2	12.5	12	17.4	5	38.0
Total anomalies	53		16		69		13	

Note. [a]Combined experience with 1,110 control embryos examined in this and other experiments during the same time period. Adapted from Smith et al., 1972.

the higher dose of ether, this dose was lethal to mice and guinea pigs but not rats for unknown reasons. The mortality was unrelated to changes in blood or the appearance of histologic changes in any tissue examined, including bone marrow. These animals did manifest gross hepatic enlargement. Perhaps ether or its metabolism to ethyl alcohol stimulated growth of the liver, but how that is related to ether lethality is unclear.

In another study, rabbits, rats and guinea pigs were exposed to 2000 ppm of diethyl ether for 7 hours per day, 5 days per week for a total of 7 weeks. During the exposures, the animals were observed for signs of possible toxicity, including alterations in activity, symptoms of eye and nasal irritation, skin condition and respiratory distress. The results of the study demonstrated no consistent increases in organ ratios, no hematological deviations, and no changes in SGOT and SGPT levels (Chenoweth, Leong, Sparschu & Torkelson, 1972).

In a study regarding exposure to lower concentrations of diethyl ether (7 hours, 5 days a week for 6-7 weeks) using rats, rabbits and guinea pigs at 1/10 minimum alveolar concentration (minimum alveolar concentration is defined as the minimum concentration in the alveolus at which 50% of subjects moved in response to skin incision [Wood & Wood, 1982]), ether was without

reported deleterious effect and compared well with the air-exposed controls (Chenoweth, 1971).

Adverse Effects from Industrial Use of Diethyl Ether

As well as an inhalation anesthetic, diethyl ether is used as a solvent for waxes, fats, oils, perfumes, alkaloids, dyes, gums, resins, nitrocellulose, hydrocarbons, raw rubber and smokeless powder; a refrigerant, in diesel fuels, in dry cleaning, as an extractant, and as a chemical reagent for various organic reactions. Yet, despite this wide industrial use, there is practically nothing in the literature about ether as an industrial poison. The literature that is available states that industrial exposure to chronic low concentrations may cause a variety of symptoms including loss of appetite, nausea, vomiting, faintness, exhaustion, headache, dizziness, drowsiness, excitation, psychic disturbances and constipation. Albuminuria has been reported (Occupational diseases, 1977) as well as polycythemia, increased white count, and occasionally slight anemia (Hamilton & Minot, 1920). Local effects of ether vapors are irritation to the eye, nose and throat, and contact to the liquid may produce a dermatitis (Occupational diseases, 1977).

Research Questions

The following research questions were considered

in this investigation:

1. Are EEG technicians exposed to diethyl ether via collodian use?

1.1 What exposure levels of diethyl ether are in the EEG technicians work environment?

2. Is there a body burden of diethyl ether in EEG technicians with exposure to low concentrations of diethyl ether?

2.1 Can diethyl ether be detected in the expired air of EEG technicians using collodian?

2.2 Does diethyl ether accumulate in the body with repeated exposure as measured by the expired air concentrations?

3. Is there a relationship between the number of EEGs performed and the amount of diethyl ether in the work environment?

4. Do detectible levels of ether in the expired air have a relationship to the amount of ether in the EEG technicians' work environment?

CHAPTER III

METHODOLOGY

The design of the study was descriptive. Air samples were collected from the breathing zone of each subject at the place of work on five consecutive days. During the same period, expired air samples were collected for each subject pre- and postwork. An expired air sample was also collected prior to work the following week.

Population

The study population was composed of 4 EEG technicians in the Salt Lake City area. All subjects were contacted via telephone and questioned as to their use of collodian. All subjects met the following criteria:

1. Currently working 40 hours per week as an EEG technician performing 2-4 electroencephalograms per day.

2. Using collodian routinely in the electroencephalogram procedure.

Instrumentation

The following instruments were employed in this investigation:

1. A questionnaire eliciting demographic information about all subjects and their use of collodian (Appendix C).

2. A personal sampling pump. Each pump was calibrated before and after each sampling period and visually checked at regular intervals during the sampling period to maintain a flow rate of 2 liters/minute.

3. Charcoal collection tube: a glass tube with both ends flame sealed containing two sections of 400/200 mesh activated charcoal separated by a 2 mm portion of urethane foam.

4. An expired air sampling device: A 5-litre saran bag with a 2-way sealable valve.

Sampling Method

1. The questionnaire responses were elicited by the researcher.

2. The personal sampling pump and charcoal collection tube were attached to each subject at the onset of work. At the end of the work day, the pump and collection tube were removed, the charcoal tube was sealed and labeled. This method was repeated each day for 5 consecutive days. A control charcoal tube was opened and sealed for analysis on each of the sampling days.

3. Expired air samples were collected by filling the 5-litre bag with approximately 3-4 vital capacity

maneuvers. When the bag was full, the subject rebreathed into the bag 3-5 times allowing for an equilibrium between alveolar air and the expired air sample. This method was repeated twice daily, before and after work for 5 consecutive days and on the morning of the following Monday.

Procedure Sequence

One week prior to sampling:

1. Informed consent form was signed by subjects.

2. Demographic information was obtained from subjects.

3. The date and times for each sampling were confirmed with the subjects.

Sample Collection

1. The morning of the first sampling day, an expired air sample was collected from subjects before exposure as per the sampling method at the subject's workplace.

2. After collection of the expired air sample, a personal pump and charcoal collection tube were attached to each subject.

3. At the end of the subject's work day, the afternoon expired air sample was collected and the charcoal collection tube removed and sealed.

4. Charcoal tube and expired air samples were

taken to the Utah Biomedical Test Laboratory at the end of each day.

5. This procedure sequence was repeated for 5 consecutive days.

6. An additional expired air sample was collected the following Monday morning.

Analysis of Samples

Samples were analyzed by Gas Chromatography at the Utah Biomedical Test Laboratory (NIOSH, Method No. 127).

CHAPTER IV

DATA ANALYSIS

Study Population

Four subjects were selected who met the criteria for inclusion in the study. The subjects ranged in age from 22-47 years. Two subjects were smokers and two nonsmokers. The number of years of collodian use ranged from 10 months to 13 years. No subject had any history of lung disease or any acute respiratory problems at the time of this study. One subject reported being on the following medications: Synthyroid and Megace.

Analysis of Sample

Both air and breath samples were analyzed by the Utah Biomedical Test Laboratory. Results of the charcoal tube samples were then converted to mg/m^3. The personal sampling pumps were calibrated before and after each sampling period and the average was used in the calculations. Refer to Appendix E for the data used in the calculations.

Data Analysis

The first research question stated:

1. Are EEG technicians exposed to diethyl ether via collodian use?

1.1 What exposure levels of diethyl ether are in the EEG technicians work environment?

Results of sample analysis demonstrate that EEG technicians are exposed to ether. Table 3 presents the levels of ether found in the EEG technicians work environment. Each sample contained a detectable amount of ether. The levels of ether ranged from 3.3 mg/m^3 to 23.6 mg/m^3 with a mean amount of 15.78 mg/m^3 and a median amount of 17.09 mg/m^3.

Research question 2 stated:

2. Is there a body burden of diethyl ether in EEG technicians with exposure to low concentrations of ether?

2.1 Can diethyl ether be detected in the expired air of EEG technicians using collodian?

2.2 Does diethyl ether accumulate in the body with repeated exposure as measured by the expired air concentrations?

All samples of expired air contained detectible levels of diethyl ether. Levels of ether in expired air samples ranged from .002 mg to .38 mg. The mean amount was .047 mg and the median was .016 mg. The expired air

Table 3

Sampling Results

Subject	Levels of Diethyl Ether in Breathing Zone Air Mg/m^3 Monday Day 1	Tuesday Day 2	Wednesday Day 3	Thursday Day 4	Friday Day 5
A	8.65	19.84	20.14	9.1	16.58
B	14.67	18.6	20.22	----	9.01
C	20.13	17.09	23.26	23.27	23.6
D	11.2	3.3	8.5	12.29	20.42

sample results are shown in Table 4. The levels of ether in expired air did not increase during the week and in fact were lower on the last day of the week than on the first. Sample results demonstrated no consistent increase in ether levels immediately after exposure. Levels of ether were lower in the afternoon immediately after exposure than in the morning 12 out of the 18 combined sampling days.

Research question 3 stated:

3. Is there a relationship between the number of EEGs performed and the amount of diethyl ether in the work environment?

The breathing zone ether levels and the number of EEGs done per day were plotted on a scatter diagram. The graph indicates a trend toward a positive relationship between these two factors (Figure 4) (correlation coefficient r=.536; 95% confidence interval .05-.8).

Research question 4 stated:

4. Do detectible levels of ether in the expired air have a relationship to the amount of ether in the EEG technicians work environment?

The environmental sample results and expired air sample results were plotted on a scatter diagram. There is no indication of a trend or relationship between the expired air and breathing zone sample results (Figure 5).

Table 4

Sampling Results

	Levels of Diethyl Ether in Expired Air Samples					
	Monday Day 1	Tuesday Day 2	Wednesday Day 3[a]	Thursday Day 4[a]	Friday Day 5[a]	Monday Day 6[a]
Subject A						
am	0.28	0.028	0.018	N.S.	0.006	0.003
pm	0.10	0.038	0.011	0.007	0.008	
Subject B						
am	0.38	0.014	0.020	0.007	0.005	0.006
pm	0.12	0.030	0.013	N.S.	0.10	
Subject C						
am	0.18	0.023	0.016	0.006	0.007	N.S.
pm	0.083	0.017	0.013	0.014	0.013	
Subject D						
am	0.11	0.044	0.020	0.007	0.009	0.002
pm	0.093	0.032	0.017	0.009	0.008	

Note. [a]These expired air results are included as reported by the laboratory. It is known that the amount of ether in the sample bags decreased over time and that analysis of these samples was delayed 1 to 7 days therefore these results are considered to be invalid.

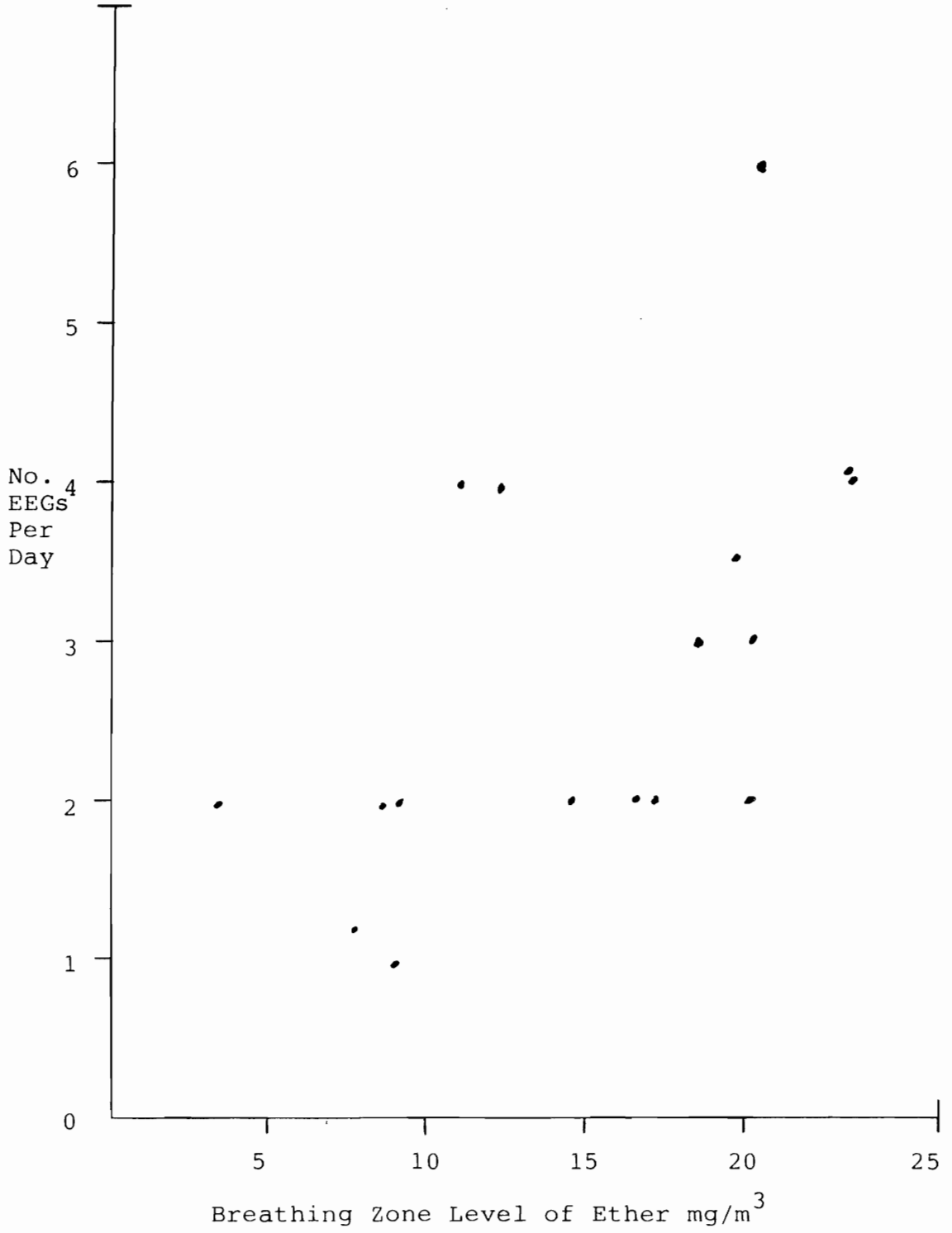

Figure 4. Number of EEGs per day and breathing zone levels.

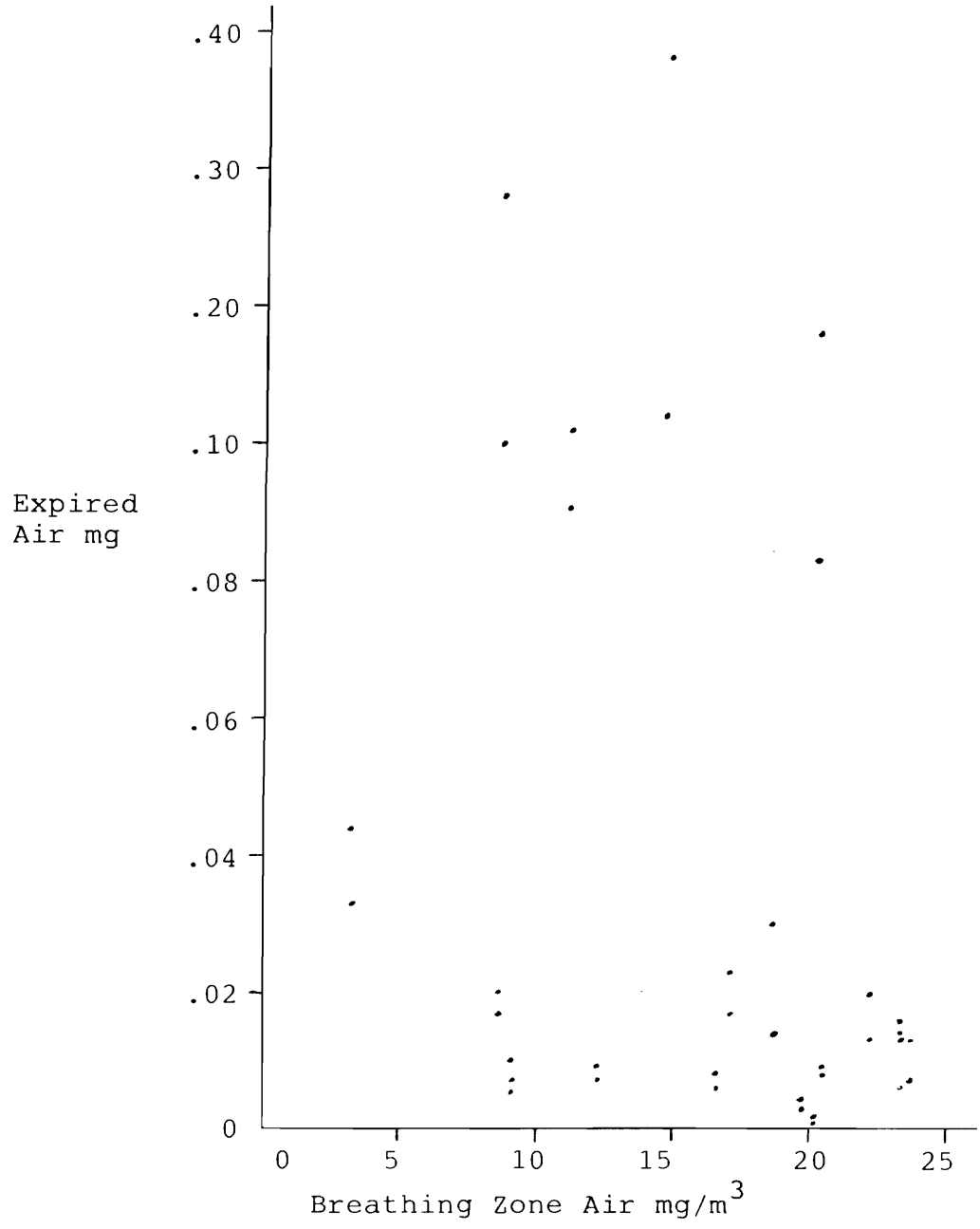

Figure 5. Breathing zone levels and expired air levels of ether.

No further statistical analysis was deemed necessary because of the randomness of the scattergram.

CHAPTER V

DISCUSSION

One conclusive finding of this study is that EEG technicians using collodian are exposed to diethyl ether. This is demonstrated by the detectible levels of ether found in the breathing zone air of the subjects. Based on the assumption that exposure during the nonsampling period was the same as during the sampling time, the levels of ether found in this study can be compared to the recommended standard for an 8-hour time weighted average of 1200 mg/m^3. The levels of ether found in this study were far below this recommended standard. However, study levels were above those recommended by the Hospital Engineering Cooperative Group of Denmark for long-term exposure of 9 mg/m^3 (NIOSH document, 1977).

A second finding of this study was that there is a direct relationship between the amount of ether found in the breathing zone air and the number of electroencephalograms that were performed by the technicians during the sampling period. A possible explanation is that the more that EEGs are performed, the more collodian use is required, hence increasing the amount of ether present in the environment. Other factors that

would influence the amount of collodian used are the number of electrodes that are applied for a particular procedure and the amount of time needed to apply the electrodes such as with a cooperative patient versus an uncooperative one. Another factor that may affect the amount of ether in the environment is the ventilation rate and room size of the EEG lab and the storage of used collodian.

The third finding of this study is that there is a body burden of diethyl ether in EEG technicians with exposure to low concentrations of ether. Detectible levels of ether were found in all samples of expired air including those collected after 2 days with no ether exposure. However, the data in this study do not show an accumulation of ether in the body with repeated exposures as measured by the expired air concentrations. There was no consistent increase in expired air levels of ether over the 5 day period of consecutive sampling. Levels in the expired air were lower on the last day of sampling than on the first day. Also, on 12 of the 18 combined sampling days ether levels were lower in the afternoon immediately after exposure than in the morning before exposure. The levels of ether on the second Monday morning after 2 days with no exposure were only slightly lower than on Friday afternoon. Possible explanations for this are:

1. The expired air sample results do not accurately reflect expired air levels in the subject.

1.1 One reason for this is the loss of ether from the collection bag. It was found during the analysis of samples that the concentration of ether in the sampling bags decreased over a period of time. The samples collected on Day 1 (Monday) were analyzed within a few hours of collection. The next day, analysis of these same samples was repeated and the ether concentration was found to be approximately 30% lower than the results from the previous day. Samples collected on the following days were analyzed 1 to 7 days later--the longest delays occurring with the samples that were collected on the third, fourth and fifth days and with the samples collected the following Monday morning. This loss of ether from the sampling bag over time would result in lower amounts of ether in the samples collected on the third, fourth and fifth days, as well as the following Monday. Several possibilities may account for the loss of ether over time.

1.1.1 One possibility is the presence of a leak from the sampling bag values or the bag walls themselves. Each of the sampling bags were checked for air tightness prior to the onset of sampling but the presence of a very slow leak cannot be excluded.

1.1.2 A second explanation may be that

the ether interacted with the bag's surface or with moisture in the sample bags which condensed on the bag surface causing a physical nonreactive absorption of the gas to the condensate. The analyst reported that during sample measuring there was extensive deposition of moisture on the inside wall of the syringes after withdrawing air from the sampling bags.

The mylar sampling bag used in this study may not be an appropriate sampling device for diethyl ether and/or the collection of expired air. A study done on this bag used vinyl chloride monomer gas to test for permeability and storage stability; it showed no loss of VCM over a period of one week. Also, it was found that after cleansing the bag with compressed air, emptying and repeating this cycle, no detectable levels of VCM were found in the bags. This study collected VCM from the breathing zone not from expired air (Levine, Hebel, Bolton & Kugel, 1975). No studies were found which tested the bag's reliability with expired air samples. Other studies regarding the collection of expired air samples used a glass sampling tube (Brugnone, Perbellini, Gaffuri & Apostoli, 1980; Pasquini, 1978; Stewart, Hake & Peterson, 1974). This instrument was not available to the researcher for this study. The research team did not determine prior to this study the mylar bag's reliability and stability in terms

of expired air samples of diethyl ether.

1.2 Invalid expired air sample results may also be attributed to problems encountered in the analytical process. Problems encountered during sample analysis were:

1.2.1 The use of nonairtight syringes to draw air from sampling bag and inject into the gas chromatograph injection port. The nonairtight syringes leaked extensively, especially when injected into the GC injection port. The extent this altered the results is not known.

1.2.2 It was not possible to obtain reproducible injections. Several injections (n=6-7) of the same sample were performed. The outliers were eliminated and the average value of median values was computed for reporting the results. The analyst used the following process to obtain samples for analysis from the sampling bags: The bags were shaken well, then 2 ml of air volume was drawn from the top side of the bag while lying horizontally in a 5 ml syringe then injected into the gas chromatograph injection port.

2. The second possible explanation is that the ether content in expired air does not reflect the amount of ether exposure. As stated in the literature review, very little is known of the metabolism and

elimination of ether especially in subjects exposed to repeated low levels of ether. One study found that a portion of administered ether was stored in fat and released slowly. As the slow release occurs, the amount of ether in the animal was maintained at a constant, although low, level (Van Dyke et al., 1964). Although this phenomenon is not clearly understood, its possible that the individual subject maintains a fairly constant body level of ether despite fluctuations in the environmental levels. This may also be influenced by an individual's metabolic and body characteristics, as well as lifestyle.

These results did not demonstrate a relationship between levels of ether in the expired air of subjects and those found in the breathing zone. Possible explanations for this are the same as those discussed earlier. The first is that the expired air sample results do not accurately reflect expired air levels in the subject and the second, the ether content in expired air does not reflect the amount of ether exposure.

Recommendations for Future Research

Since it has been determined that EEG technicians using collodian are exposed repeatedly to low concentrations of ether and a body burden of ether does exist from this exposure, it is recommended that EEG technicians using collodian be added to the list of occupations

with potential ether exposure. The long-term effects of low concentrations of ether are not known; therefore, levels in the environment should be kept as low as possible. This should be taken in consideration in the construction of EEG labs, in the engineering of air flow and ventilation in these areas, and in work practice techniques.

Because of the invalid expired air sample results, no recommendations can be made regarding the accumulation of diethyl ether in the body with repeated exposure or the relationship between expired air concentrations and breathing zone air levels of diethyl ether.

This study was limited by the paucity of knowledge regarding the sampling and analysis of ether in expired air as well as the biotransformation and elimination of ether from the body. Before replication of this type of study is attempted, additional data on the following areas would be useful:

1. Additional studies on the reliability and validity of various sampling instruments to determine expired air levels of ether. One instrument that could be considered for this sampling is the charcoal sampling tube. Its "Limit of Detection" (LOD) as reported on the breathing zone air samples was .01 mg. If the first day of expired air sample results in this study are considered the most accurate, this LOD would be far below

the levels of ether in expired air. It is recommended that in future studies of this type, analysis of samples be performed within a few hours of sampling if the reliability and stability of the sampling instrument cannot or has not been determined.

2. Research on the metabolism and elimination of ether through the respiratory system to arrive at a reliable breath decay curve. Studies comparing the elimination of diethyl ether through the respiratory system after repeated exposures to low concentrations of ether and elimination of ether after isolated exposure to higher concentrations to determine if biotransformation and elimination is dose affected.

3. Research on other biological monitoring methods, such as blood and tissue sampling.

Future areas of research might include the longitudinal study of long-term exposure to ether, at both high and low concentrations. Subjects with high exposure levels may give earlier indications of adverse effects and the reliability of sampling methods. Subjects with low exposure levels may provide information especially relevant to the usual hospital or clinic work setting, and may serve to evaluate, develop, or revise the present occupational standards.

Conclusion

A general statement can be made that EEG technicians

who use collodian are exposed to diethyl ether. Levels found in this study were below the recommended TLV of 400 ppm. However, no studies were available regarding the effects of long-term exposure to low concentrations of ether. EEG technicians who use collodian may be a good population to study regarding possible effects of long-term exposure. In terms of using expired air sampling to study exposure to ether, more data need to be acquired. A sampling instrument needs to be tested for it's validity and reliability. Also, more information is needed regarding the metabolism and elimination of ether, the breath decay curve of ether, as well as other methods of biological testing for ether exposure.

APPENDIX A

CONSENT FORMS

SUBJECT INFORMATION

AND

INFORMED CONSENT FORM

Information about "Diethyl Ether Exposure to EEG Technicians Using Collodian" study:

The purpose of this study is to determine if EEG technicians using collodian are exposed to low concentrations of diethyl ether and to determine if diethyl ether is accumulated in the body with repeated exposures.

Levels of diethyl ether in the breathing zone air of EEG technicians will be determined as well as levels of ether in expired air. A personal sampling pump and charcoal collection tube will be attached to the EEG technician for 8 hours on 5 consecutive days. Expired air samples will be collected in a 5-litre bag twice a day, pre and postwork. Environmental monitoring and sample collection will be done for 5 consecutive days. A final expired air sample will be collected prework on the following Monday. All sampling instruments will be delivered to and collected at the subject's workplace.

Details of this study have been discussed with the subject and an opportunity given to ask questions regarding the study and participation in this study. If there are any questions before or during the study, participants are free to contact Jeri Lockman at 485-3995.

The risk involved in participating in this study is the one-half to one hour per day of the subject's time. Sample collection will be done at the workplace and coordinated prior to the onset of the study.

Benefits of this study will be an increased knowledge regarding ether levels in the environment and expired air from the use of collodian.

All samples will be coded so as to insure confidentiality.

The subjects are free to withdraw from this study at any time without prejudice to themselves.

_____

Subject

_____

Date

APPENDIX B

INFORMED CONSENT PROCEDURE FORM

Informed Consent Procedure

1. Each subject will be given information regarding the nature of this study and study objectives.

2. A detailed description of the sampling methods will be explained to the subjects. A personal sampling pump, charcoal collection tube and expired air sampling bag will be shown and a demonstration of its use given at this time.

3. The sample procedure will be described. The exact times for sample collection will be coordinated with each subject so as to eliminate any interference with the subject's work schedule. Samples will be collected at the workplace to eliminate travel expense and time for the subjects. The amount of time involved will be approximately one-half to one hour per day for each subject.

4. Potential benefits of this study will be discussed with each subject. Benefits include increased knowledge regarding collodian use and the level of diethyl ether in the air.

5. Each subject will be informed of his/her right to withdraw from the study at any time without prejudice to him/herself.

6. Each subject will be given an opportunity to ask questions regarding the study and any procedure in the study.

7. All samples will be coded so as to insure confidential handling. Subjects may be given results of their individual samples upon request.

8. An informed consent form will be signed by each subject agreeing to participate in this study.

APPENDIX C

PRESAMPLING QUESTIONNAIRE

Name: _____ Subject Code: _____

Sex: Male _____ Female _____ Age _____

History of lung disease (asthma, bronchitis) _____

_____

Smoker: _____ Nonsmoker: _____

Medications: _____

Hours worked per week with collodian: _____

Number of years of collodian use: _____

How is collodian stored: _____

Where is collodian stored: _____

How is collodian disposed of: _____

APPENDIX D

SAMPLING RECORD

Sampling Record

Subject Code: _____

Day 1

Expired air collection time: Sample A1____ Sample B1____

Personal Sampling Pump: On____ Off____

No. of EEGs_____ Time of last EEG _____

Day 2

Expired air collection time: Sample A2____ Sample B2____

Personal Sampling Pump: On____ Off____

No. of EEGs_____ Time of last EEG _____

Day 3

Expired air collection time: Sample A3____ Sample B3____

Personal Sampling Pump: On____ Off____

No. of EEGs_____ Time of last EEG _____

Day 4

Expired air collection time: Sample A4____ Sample B4____

Personal Sampling Pump: On____ Off____

No. of EEGs_____ Time of last EEG _____

Day 5

Expired air collection time: Sample A5____ Sample B5____

Personal Sampling Pump: On____ Off____

No. of EEGs_____ Time of last EEG _____

Day 6

Expired air collection time: Sample A6____

APPENDIX E

ENVIRONMENTAL SAMPLE CONVERSION DATA

Subject A

Sampling Time	6hr 38min	6hr 41min	5hr 44 min	6hr 31min	6hr 25min
Sample Result	5.3 mg	14 mg	9.7 mg	6.9 mg	12 mg
Flow Rate	1.54 1 pm	1.76 1 pm	1.4 1 pm	1.94 1 pm	1.84 1 pm

Subject B

Sampling Time	6hr 40min	6hr 24min	6hr 25min	--	5hr 55min
Sample Result	8.8 mg	13 mg	13 mg	--	6.4 mg
Flow Rate	1.5 1 pm	1.82 1 pm	1.67 1 pm	--	2 1 pm

Subject C

Sampling Time	6hr 39min	6hr 49min	7hr 20min	7hr 05min	7hr 25min
Sample Result	13 mg	10 mg	18 mg	18 mg	21 mg
Flow Rate	1.62 1 pm	1.43 1 pm	1.76 1 pm	1.82 1 pm	2 1 pm

Subject D

Sampling Time	7hr 21min	7hr 30min	7hr 45min	7hr 56min	7hr 45min
Sample Result	8 mg	2.7 mg	6.4 mg	11 mg	15 mg
Flow Rate	1.62 1 pm	1.82 1 pm	1.62 1 pm	1.88 1 pm	1.58 1 pm

APPENDIX F

INFORMATION ON COLLODIAN

U.S. Coast Guard
Chemical Hazards Response Information System (Chris)
9-11-78

CLD COLLODION

Common Synonyms

Cellulose nitrate solution Nitrocellulose solution Pyroxylin solution Box toe gum Nitrocellulose gum	Thick liquid	Colorless	Ether-like odor

Floats on water. Flammable, irritating vapor is produced. Boiling point is around 94°F.

Shut off ignition sources. Call fire department.
Stop discharge if possible.
Isolate and remove discharged material.
Notify local health and pollution control agencies.

Fire

FLAMMABLE.
POISONOUS GASES MAY BE PRODUCED IN FIRE.
Containers may explode in fire.
Flashback along vapor trail may occur.
Vapor may explode if ignited in an enclosed area.
Extinguish with dry chemicals, alcohol foam, or carbon dioxide.
Cool exposed containers with water.

Exposure

Call for medical aid.
VAPOR
Irritating to eyes, nose and throat.
If inhaled will cause dizziness, difficult breathing, or loss of consciousness.
Move victim to fresh air.
If breathing has stopped, give artificial respiration.
If breathing is difficult, give oxygen.
LIQUID
Not harmful.

Water Pollution

Effect of low concentrations on aquatic life is unknown.
Fouling to shoreline.
May be dangerous if it enters water intakes.
Notify local health and wildlife officials.
Notify operators of nearby water intakes.

1. Response to Discharge (See Response Methods Handbook, CG446-4).

   Issue warning, high flammability
   Restrict access
   Mechanical containment
   Should be removed
   Chamical and physical treatment

2. Label

3. Chemical Designations

   3.1 Synonyms: Cellulose nitrate solution; nitrocellulose solution; pyroxylin solution; box toe gum; nitrocellulose gum.

   3.2 Coast Guard compatability classification: Not applicable.

   3.3 Chemical Formula: Not pertinent.

   3.4 IMCO/United Nations Numerical Designation: 3.2/2059.2061 3.3/2060.2062

4. Observable Characteristics

   4.1 Physical State (as shipped); Viscous liquid.

   4.2 Color: Colorless.

   4.3 Odor: Depends on solvent used; often that of ether.

5. Health Hazards

   5.1 Personal Protective Equipment: Self-contained breathing apparatus; rubber gloves; goggles or face shield.

   5.2 Symptoms Following Exposure: High concentration of ether fumes may cause narcosis, loss of consciousness and respiratory paralysis if inhaled. Contact with eyes causes irritation.

   5.3 Treatment for Exposure: INHALATION: remove victim to fresh air; initiate artificial respiration if breathing has stopped; call physician.

5.4 Toxicity by inhalation (Threshold Limit Value): 400 ppm>

5.5 Short-Term Inhalation Limits: Data not available.

5.6 Toxicity by Ingestion: Grade 0: LD_{30} >15 g/kg.

5.7 Late Toxicity: Data not available.

5.8 Vapor (Gas) Irritant Characteristics: Vapors cause a slight smarting of the eyes or respiratory system if present in high concentrations. The effect is temporary.

5.9 Liquid or Solid Irritant Characteristics: No appreciable hazard. Practically harmless to the skin.

5.10 Odor Threshold: Data not available.

6. Fire Hazards

6.1 Flash Point: -49°F C.C. (ether)

6.2 Flammable Limits in Air: 1.9%-36% (ether solution).

6.3 Fire Extinguishing Agents: Dry chemical, alcohol foam, carbon dioxide.

6.4 Fire Extinguishing Agents Not to be Used: Water may be ineffective.

6.5 Special Hazards of Combusion Products: The formation of extremely toxic gases, notably oxides of nitrogen, hydrogen cyanide, and carbon monoxide is possible.

6.6 Behavior in Fire: Highly flammable solvent vapors are formed. May travel a long distance to a source of ignition and flash back.

6.7 Ignition Temperature: 356°F (ether).

6.8 Electrical Hazard: Class I, Group C.

6.9 Burning Rate: Data not available.

7. Chemical Reactivity

   7.1 Reactivity with Water: No reaction.

   7.2 Reactivity with Common Materials: No reaction.

   7.3 Stability During Transport: Stable.

   7.4 Neutralizing Agents for Acids and Caustics: Not pertinent.

   7.5 Polymerization: Not pertinent.

   7.6 Inhibitor of Polymerization: Not pertinent.

8. Water Pollution

   8.1 Aquatic Toxicity: Data not available.

   8.2 Waterfowl Toxicity: Data not available.

   8.3 Biological Oxygen Demand (BOD): Data not available.

   8.4 Food Chain Concentration Potential: None.

9. Selected Manufacturers

   1. Mallinckrodt Chemical Works
      Second and Mallinckrodt Streets
      St. Louis, MO 63160

   2. Polysciences, Inc.
      Paul Valley Industrial Park
      Warrington, PA 18976

10. Shipping Information

   10.1 Grades or Purity: USP. All grades contain less than 60% nitrocellulose by weight.

   10.2 Storage Temperature: Ambient.

   10.3 Inert Atmosphere: No requirement.

   10.4 Venting: Pressure-vacuum/

11. Hazard Assessment Code (See Hazard Assessment Handbook, CG 446-3) A-T-U-V-W.

12. Hazard Classifications

12.1 Code of Federal Regulations: Flammable liquid.

12.2 NAS Hazard Rating for Bulk Water Transportation:

Category	Rating
Fire	4
Health	
Vapor Irritant	1
Liquid or Solid Irritant	0
Poisons	2
Water Pollution	
Human Toxicity	0
Aquatic Toxicity	1
Aesthetic Effect	1
Reactivity	
Other Chemicals	1
Water	0
Self-Reaction	0

12.3 NFPA Hazard Classifications:

Category	Classification*	
Health Hazard (Blue)	0	2
Flammability (Red)	3	3
Reactivity (Yellow)	3	3

*First column refers to nonfire situation.

13. Physical and Chemical Properties

13.1 Physical State at 15°C and 1 atm: Liquid.

13.2 Molecular Weight: Not pertinent.

13.3 Boiling Point at 1 atm: 93°F = 34°C = 307°K (ether solvent)

13.4 Freezing Point: Not pertinent.

13.5 Critical Temperature: Not pertinent.

13.6 Critical Pressure: Not pertinent.

13.7 Specific Gravity: 0.772 at 25°C (liquid).

13.8 Liquid Surface Tension: Not pertinent.

13.9 Liquid-Water Interfacial Tension: Not pertinent.

13.10 Vapor (Gas) Specific Gravity: Not pertinent.

13.11 Ratio of Specific Heats of Vapor (Gas): Not pertinent.

13.12 Latent Heat of Vaporization: Not pertinent.

13.13 Heat of Combustion: Data not available.

13.14 Heat of Decomposition: Not pertinent.

13.15 Heat of Solution: Not pertinent.

13.16 Heat of Polymerization: Not pertinent.

Notes

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